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Dr. David Stone
Council for Tobacco Research
900 3rd Avenue, NY, NY 10022

October 10, 1992


Dear Dr. Stone,

I have just recently been appointed to a faculty position as Senior Lecturer in the Technion Medical School. Professors Aharon Razin and Howard Cedar at The Hebrew University suggested that I write you a letter inquiring whether my topic of research is suitable for funding by the Tobacco Research Foundation. The focus of the work in my lab will be to study the role of transcription factors in directing morphogenesis and differentiation in the developing vertebrate embryo. I have been examining the regulation and function of POU homeobox and basic Helix-Loop-Helix DNA binding proteins in the amphibian - *Xenopus laevis*. The amphibian embryo is large and easily manipulated, I have utilized microinjection of biologically active mRNA into embryos to directly address questions regarding gene function during embryogenesis *in vivo*.

One of the major challenges facing biologists is the difficulty in understanding how a fertilized egg maintains the molecular capacity to differentiate into a multicellular organism of 10^{15} cells. Developing cells must communicate with one another and respond to environmental cues to undergo proper spatial organization and tissue differentiation. The orchestration of this tissue morphogenesis occurs during embryogenesis. Cancer is a disease in which differentiated somatic cells lose their normal developmental and morphogenetic behaviours. The molecular pathways regulating these normal morphogenetic and developmental pathways in vertebrates are poorly understood. Many of these events occur during the earliest stages of development which I have been studying in the amphibian. Elucidation of the basic mechanisms directing these early developmental cellular processes would likely aid in understanding what actually goes wrong in a normal cell when it becomes cancerous. Better understanding of the normal molecular processes of cellular morphogenesis will shed new light on the problem of better

understanding cancer cell behaviour; and perhaps will aid in designing strategies for returning tumour cells to their normal developmental program. If you feel that this work has potential for funding by the Tobacco Foundation, I would like to receive a grant application.

Sincerely Yours,

A handwritten signature in cursive script, appearing to read "Dale Frank". The signature is written in dark ink and is positioned above the printed name.

Dr. Dale Frank